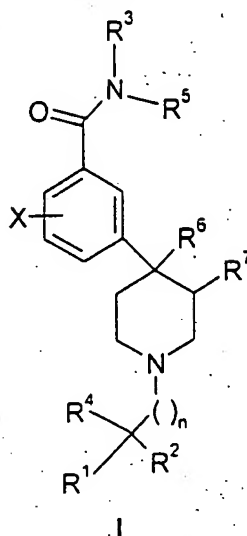


Claims:

1. A compound according to formula I:



wherein X is H, halogen, or CN;

- 5 R^1 and R^2 are independently H, C_1 - C_6 alkyl, $-(CH_2)_k$ -aryl, $-(CH_2)_k$ -heteroaryl, wherein said alkyl, $-(CH_2)_k$ -aryl or $-(CH_2)_k$ -heteroaryl group is optionally substituted anywhere on said group with one or more R^{12} groups, or, with the carbon to which R^1 and R^2 are attached, are connected to form a C_3 - C_7 cycloalkyl or a 4-7 membered carbocyclic or heterocycloalkyl comprising from one to three hetero moieties selected from O, S, $-C(=O)$, and N; and wherein
10 said cycloalkyl or heterocycloalkyl optionally contains one or more double bonds; and wherein said cycloalkyl or heterocycloalkyl is optionally fused to or substituted with a C_6 - C_{14} aryl or 5-14 membered heteroaryl group; wherein said C_3 - C_7 cycloalkyl or 4-7 membered carbocyclic or heterocycloalkyl formed by R^1 and R^2 can each optionally be substituted by from one to three R^{12} groups, and said optionally fused or substituted aryl or heteroaryl, substituted alkyl,
15 substituted aryl optionally fused aryl or heteroaryl may each optionally independently be substituted with from one to six R^{12} groups in any stereochemical relationship;

- wherein the R^{12} groups are independently selected from H, R^{13} , R^{16} , $-C_1$ - C_4 alkyl optionally containing one or two unsaturated bonds, halogen, $-OR^{13}$, $-NO_2$, $-CN$, $-C_3$ - C_6 cycloalkyl, aryl, substituted aryl, wherein said aryl or substituted aryl is independently
20 optionally substituted with 1-3 R^{18} groups, $-C(R^4)(C_1$ - C_4 alkyl)(C_1 - C_4 alkyl) wherein said alkyl groups may form a C_3 - C_7 carbocyclic ring, $-(CH_2)_n$ - $NR^{13}R^{14}$, $-NR^{13}C(=O)R^{14}$, $-C(=O)NR^{13}R^{14}$, $-OC(=O)R^{13}$, $-C(=O)OR^{13}$, $-C(=O)R^{13}$, $-NR^{13}C(=O)OR^{14}$, $-NR^{13}C(=O)NR^{14}R^{15}$, $-NR^{13}S(=O)_2R^{14}$, $-NR^{17}S(=O)_2NR^{13}R^{14}$ and $-S(=O)_2R^{13}$;

- R^{18} is H, F, Cl, $-OH$, $-C_1$ - C_4 alkyl, $-C\equiv N$, $-NR^{13}C(=O)R^{14}$, $-C(=O)NR^{13}R^{14}$, $-O(C_1$ -
25 C_4)alkyl, $-NH(C_1$ - C_4 alkyl), $-N(C_1$ - C_4 alkyl)(C_1 - C_4 alkyl), $-(CH_2)_nOH$, $-(CH_2)_n$ - $C\equiv N$, $-(CH_2)_n$ -

$\text{NR}^{13}\text{C}(=\text{O})\text{R}^{14}$, $-(\text{CH}_2)_n\text{C}(=\text{O})\text{NR}^{13}\text{R}^{14}$, $-(\text{CH}_2)_n\text{O}(\text{C}_1\text{-C}_4)\text{alkyl}$, $-(\text{CH}_2)_n\text{NH}_2$, $-(\text{CH}_2)_n\text{NH}(\text{C}_1\text{-C}_4\text{ alkyl})$ or $-(\text{CH}_2)_n\text{N}(\text{C}_1\text{-C}_4\text{ alkyl})(\text{C}_1\text{-C}_4\text{ alkyl})$;

R^4 is absent or is H, $-\text{C}_1\text{-C}_4$ alkyl which may optionally contain one or two unsaturated bonds, $-\text{OH}$, $\text{O}(\text{C}_1\text{-C}_4)\text{alkyl}$, $(\text{C}_1\text{-C}_4)\text{-alkyl-OH}$, $(\text{CH}_2)_n\text{NH}_2$, $-(\text{CH}_2)_n\text{NH}(\text{C}_1\text{-C}_4\text{ alkyl})$, $(\text{CH}_2)_n\text{N}(\text{C}_1\text{-C}_4)\text{alkyl}(\text{C}_1\text{-C}_4)\text{alkyl}$, $-(\text{CH}_2)_n\text{NHC}(=\text{O})(\text{C}_1\text{-C}_4\text{ alkyl})$, $-(\text{CH}_2)_n\text{NO}_2$, $-(\text{CH}_2)_n\text{C}\equiv\text{N}$, $-(\text{CH}_2)_n\text{C}(=\text{O})\text{NH}_2$, $-(\text{CH}_2)_n\text{C}(=\text{O})\text{NH}(\text{C}_1\text{-C}_4\text{ alkyl})$ or $-(\text{CH}_2)_n\text{C}(=\text{O})\text{N}(\text{C}_1\text{-C}_4\text{ alkyl})(\text{C}_1\text{-C}_4\text{ alkyl})$, CN , NO_2 , $-\text{OR}^{16}$;

R^3 and R^5 are independently H, alkyl $\text{C}_1\text{-C}_6$, substituted alkyl $\text{C}_1\text{-C}_6$, cycloalkyl $\text{C}_1\text{-C}_6$ and substituted cycloalkyl $\text{C}_1\text{-C}_6$, $(\text{C}_2\text{-C}_4)\text{alkyl-O}(\text{C}_1\text{-C}_4)\text{alkyl}$, $(\text{C}_2\text{-C}_4)\text{alkyl-NH}(\text{C}_1\text{-C}_4\text{ alkyl})$, $(\text{C}_2\text{-C}_4)\text{alkyl-N}(\text{C}_1\text{-C}_4\text{ alkyl})(\text{C}_1\text{-C}_4\text{ alkyl})$, $(\text{C}_1\text{-C}_4)\text{alkyl-heterocyclic}$;

R^6 and R^7 are independently $\text{C}_1\text{-C}_4$ alkyl;

each R^{13} , R^{14} , and R^{15} are independently selected from H, $-\text{C}_1\text{-C}_4$ alkyl, $-(\text{C}_2\text{-C}_4\text{ alkyl})\text{O}(\text{C}_1\text{-C}_4\text{ alkyl})$, $-(\text{CH}_2)_v\text{NR}^{16}\text{R}^{17}$, or a 4- to 7-membered heterocyclic group; or R^{13} and R^{14} when in $-\text{NR}^{13}\text{R}^{14}$, may optionally be connected to form a 4 to 6 membered heterocyclic group, which heterocyclic group optionally comprises from 1 to 3 further hetero moieties selected from N, S, O and $-\text{C}(=\text{O})$;

R^{16} and R^{17} are independently H, $\text{C}_1\text{-C}_6$ alkyl or together may form a 4- to 7-membered heterocyclic group;

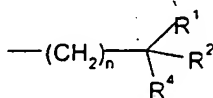
k is an integer selected from zero, 1, 2, 3, 4, and 5; and

v is an integer selected from 2, 3, 4, and 5; and

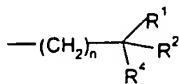
n is an integer selected from zero, 1, 2, 3, 4, and 5;

and pharmaceutically acceptable salts thereof;

with the proviso that;



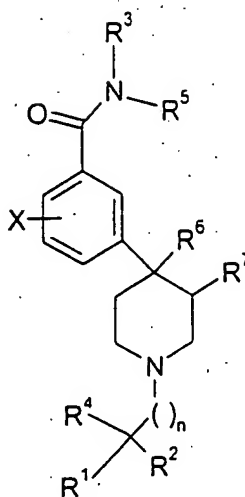
a) in said group, when n is 0, R^1 , R^2 or R^4 cannot be a heteroatom or contain a heteroatom which is directly linked to the carbon of said



group when said carbon is sp^3 hybridized; and

b) R^{13} and R^{14} cannot be H in a $-\text{NHS}(=\text{O})_2\text{R}^{14}$ or a $-\text{SO}_2\text{R}^{13}$ group.

2. The compound according to claim 1 represented by the chemical structure II:



II

Wherein each of X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷ and n is represented as described in claim 1 and the preferred relative stereochemistry between R⁶ and R⁷ is *trans*:

3. The compound according to claim 2 wherein R³ and R⁵ are H.
- 5 4. The compound according to claim 2 wherein X is H.
5. The compound according to claim 2 wherein R⁶ and R⁷ are each CH₃.
6. The compound according to claim 2 wherein n is 1, 2 or 3.
7. The compound according to claim 2 wherein R⁴ is OH, CH₂OH, NH₂, NHCOCH₃ or CN.
- 10 8. The compound according to claim 2 wherein R¹ and R² together with the carbon to which they are attached form a carbocyclic group fused to a phenyl group, an unsubstituted or substituted carbocyclic group.
9. The compound according to claim 6 wherein n is 1.
10. The compound according to claim 7 wherein R⁴ is OH.
- 15 11. The compound according to claim 2 wherein R¹ and R² together with the carbon to which they are attached form an indane ring system, a cyclobutane, cyclopentane or cyclohexane group.
12. The compound according to claim 2 wherein R¹ and R² together with the carbon to which they are attached form an indane ring system or a cyclobutane group which is substituted with a phenyl group which is unsubstituted or substituted with one or more R¹² groups.
- 20 13. The compound according to claim 1 wherein R³ and R⁵ are H, X is hydrogen, R⁶ and R⁷ are CH₃, n is 1, R⁴ is OH, CH₂OH, NH₂, NHCOCH₃ or CN and R¹ and R² together with the carbon to which they are attached, form a carbocyclic group fused to a phenyl ring or
- 25 an unsubstituted or substituted carbocyclic group.

14. The compound according to claim 2 wherein R^3 and R^5 are H, X is hydrogen, R^6 and R^7 are CH_3 , n is 1, R^4 is OH, CH_2OH , NH_2 , $NHCOCH_3$ or CN and R^1 and R^2 together with the carbon to which they are attached, form a carbocyclic group fused to a phenyl ring or an unsubstituted or substituted carbocyclic group.

5 15. The compound according to claim 14 wherein R^4 is OH and R^1 and R^2 together with the carbon to which they are attached form an indane ring system or a cyclobutane group which is substituted with a phenyl group which is unsubstituted or substituted with one or more R^{12} groups.

10 16. The compound according to claim 14 wherein R^4 is OH and R^1 and R^2 together with the carbon to which they are attached form an indane ring system.

17. The compound according to claim 14 wherein R^4 is OH and R^1 and R^2 together with the carbon to which they are attached form a cyclobutane group which is substituted with a phenyl group which is unsubstituted or substituted with one or more R^{12} groups.

15 18. The compound:

- (+/-)-3-(trans-3,4-Dimethyl-1-phenethyl-piperidin-4-yl)-benzamide;
- (+/-)-3-(1-Indan-2-ylmethyl-trans-3,4-dimethyl-piperidin-4-yl)-benzamide;
- (+/-)-3-[1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[2-(4-Methoxy-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- 20 (+/-)-3-[1-[2-(2-Methoxy-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[2-(3-Methoxy-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[trans-3,4-Dimethyl-1-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[2-(4-Cyano-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+)-3-[1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- 25 (-)-3-[1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[2-(3-Bromo-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[2-(4-Chloro-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[2-(3-Chloro-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[2-(3-Cyano-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- 30 (+/-)-3-[1-[2-(2,6-Dichloro-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[trans-3,4-Dimethyl-1-(2-pyridin-2-yl-ethyl)-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-(2-Hydroxy-2-phenyl-ethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[3-(1-Cyano-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[3-(1-Hydroxy-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- 35 (+/-)-3-[1-[3-(1-Methoxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+/-)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (+)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- (-)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;
- 40 (+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide;

- (+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide mesylate ;
 (+)-3-[1-[2-(2-Hydroxy-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-[2-[3-(1-Hydroxy-cyclohexyl)-phenyl]-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-
 benzamide ;
 5 (+)-3-[1-(cis-1-Hydroxy-3-phenyl-cyclobutylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide
 (+)-2-[4-(3-Carbamoyl-phenyl)-trans-3,4-dimethyl-piperidin-1-yl]-ethyl]-indan-2-carboxylic
 acid amide ;
 (+)-3-[trans-3,4-Dimethyl-1-[3-(2-nitro-indan-2-yl)-propyl]-piperidin-4-yl]-benzamide ;
 10 (+)-3-[1-[3-(2-Amino-indan-2-yl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-[cis-3-(4-Bromo-phenyl)-1-hydroxy-cyclobutylmethyl]-trans-3,4-dimethyl-piperidin-4-yl]-
 benzamide ;
 (+)-3-[1-[cis-1-Hydroxy-3-(4-methoxy-phenyl)-cyclobutylmethyl]-trans-3,4-dimethyl-piperidin-4-
 yl]-benzamide ;
 15 (+)-3-[1-[2-(2-Amino-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-[2-(2-Acetylamino-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-2-[4-(3-Carbamoyl-phenyl)-trans-3,4-dimethyl-piperidin-1-yl]-ethyl]-indan-2-carboxylic
 acid , or a pharmaceutically acceptable salt of any of the above-listed compounds.
 20 19. (+/-)-3-(trans-3,4-Dimethyl-1-phenethyl-piperidin-4-yl)-benzamide;
 (+/-)-3-(1-Indan-2-ylmethyl-trans-3,4-dimethyl-piperidin-4-yl)-benzamide;
 (+/-)-3-[1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+/-)-3-[trans-3,4-Dimethyl-1-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperidin-4-yl]-benzamide ;
 (+/-)-3-[1-[2-(4-Cyano-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 25 (+/-)-3-[1-(2-Hydroxy-2-phenyl-ethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+/-)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-
 benzamide ;
 (+)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 30 (+)-3-[1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide mesylate ;
 (+)-3-[1-[2-(2-Hydroxy-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-(cis-1-Hydroxy-3-phenyl-cyclobutylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide
 35 ;
 (+)-3-[1-[cis-1-Hydroxy-3-(4-methoxy-phenyl)-cyclobutylmethyl]-trans-3,4-dimethyl-piperidin-4-
 yl]-benzamide, or a pharmaceutically acceptable salt of any of the above-listed compounds.

20. A pharmaceutical composition comprising an effective amount of a
 40 compound according to any of claims 1-19 in combination with a pharmaceutically acceptable
 carrier, excipient or additive.

21. A method of treating in a mammal, in need thereof, a disease state, disorder or condition mediated by an opioid receptor or receptors which method comprises administering to said mammal an amount of a compound according to any of claims 1-19 effective in modulating an opioid receptor or receptors.

5 22. A method of treating in a mammal, in need thereof, a disease state, disorder or condition selected from the group consisting of irritable bowel syndrome, constipation, nausea, vomiting, pruritic dermatoses, psoriasis; eczema; an insect bite; an eating disorder, depression, anxiety, schizophrenia; drug addiction, an opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's
10 disease, age-related cognitive decline and Attention Deficit and Hyperactivity Disorder which method comprises administering to said mammal an amount of a compound according to any of claims 1-19 effective in treating said disease state, disorder or condition.

23. A method of treating in a mammal, in need thereof, a disease state, disorder or condition selected from the group consisting of irritable bowel syndrome, drug addiction,
15 depression, anxiety, schizophrenia and eating disorders which method comprises administering to said mammal an amount of a compound according to any of claims 1-19 effective in treating said disease state, disorder or condition.

24. A method of treating in a mammal, in need thereof, a disease state, disorder or condition selected from the group consisting of allergic dermatitis, contact dermatitis,
20 anorexia, bulimia, obesity, alcohol addiction, amphetamine addiction, cocaine addiction, morphine addiction, opium addiction, heroin addiction, erectile dysfunction and impotence, which method comprises administering to said mammal an effective amount of a compound according to any of claims 1-19 for treating said disease state, disorder or condition.

25. Use of a compound according to any of claims 1-19 in the manufacture of a
25 medicament for the treatment of a mammal.

26. Use of a compound according to any of claims 1-19 in the manufacture of a medicament for the treatment of a mammal, in need thereof, of a disease state, disorder or condition selected from the group consisting of irritable bowel syndrome, constipation, nausea, vomiting, pruritic dermatoses, psoriasis, eczema; an insect bite; an eating disorder,
30 depression, anxiety, schizophrenia; drug addiction, an opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's disease, age-related cognitive decline and Attention Deficit and Hyperactivity Disorder.

27. Use of a compound according to any of claims 1-19 in the manufacture of a medicament for the treatment of a mammal, in need thereof, of a disease state, disorder or
35 condition selected from the group consisting of allergic dermatitis, contact dermatitis, anorexia, bulimia, obesity, alcohol addiction, amphetamine addiction, cocaine addiction, morphine addiction, opium addiction, heroin addiction, erectile dysfunction and impotence.

28. A compound according to claim 1 wherein one or more atoms thereof have an atomic mass or mass number different from the atomic mass or mass number usually found in nature, or a pharmaceutically acceptable salt of such compound.

29. A method for obtaining an image of opioid receptors in a mammalian subject,
5 which method comprises administering to said subject an amount of a compound according to claim 28, or pharmaceutically acceptable salt thereof, effective in imaging opioid receptors in said subject.